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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/306,006	05/06/1999	ANDREAS WERNER SUPERSAXO	NB/2-21551/A	2914

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EXAMINER

SHARAREH, SHAHNAM J

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 04/23/2003

93

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/306,006

Applicant(s)

SUPERSAXO ET AL.

Examiner

Shahnam Sharareh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12/20/02, 2/03/ 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2, 6, 10, 15-21, 24, 28 and 29 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2, 6, 10, 15-21, 24, 28-29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 20, 2002 has been entered.

Claims 2, 6, 10, 15-21, 24, 28-29 are pending in this application. Claims 28 and 29 are independent claims. Applicants are requested to provide a clean copy of all pending claims in response to this Office Action

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 6, 10, 15-21, 24, 28-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yiv et al US Patent 6,245,349 in view of Weder WO 96/37192.

The instant claims are directed to aqueous nanodispersion formulations and methods of preparing them wherein the formulations consisting essentially of (a) 0.1-30% by weight of phospholipid (b) 1-50% by weight of polyoxyethylene co emulsifier (c) 0.1-80% by weight of a lipophilic component which comprise a natural or synthetic or a partially synthetic C₄- C₁₈ triglyceride and a lipophilic active agent in which aqueous nanodispersion, any pharmaceutically active agent is lipophilic and the active agent is always present in component (c), (d) 0.63-1.42% by weight ethanol, wherein the sum of (a), (b), (c) and (d) is 100% weight, and the formulation further contains a water phase.

Yiv et al disclose drug delivery compositions comprising particles having a size below about 50 nm diameter, and further comprising a lipophilic drug, a phospholipid (Centrophase 31), a polyoxyethylene co emulsifier (Tween 80 which is polyoxyethylene (20) sorbitan monoloeate), and a lipophilic component comprising triglycerides or

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propylene glycol diester oils having C₆ to C₁₄ for the total of 100% weight. Yiv's compositions can further be diluted with water to form an o/w emulsion (see col 5, lines 5-10, 50-65; col 6, lines 5-20, 38-65; col 9, lines 10, lines 14-60, tables 1.3, 3.1, 5.1; col 15-16, claims 1-8). The concentrations of each of Yiv's components falls within the instantly claimed ranges (see tables 1.3, 3.1, 5.1; claims 1-8). Yiv uses methods which do not need for high shear mixing equipments (see col 8, lines 20-28, col 10, lines 15-25). Yiv further teaches that lower alcohols such as ethanol may be used in his compositions (col 7, lines 10-14). However, Yiv fails to specifically disclose a compositions containing ethanol.

'192 patent primarily teaches similar type of nanodispersion compositions comprising phospholipid, polyoxyethylene, a lipophilic component, ethanol, a triglyceride, and a therapeutic agent. '192 also provides that the use of triglycerides improves stability and solubility of lipophilic drug in an aqueous emulsion system is conventional (see entire document, claims 1-5). '192 further teaches that it is well within purview of an ordinary skill in the art to select a suitable carrier system for the intended pharmaceutical and cosmetic use. '192 patents are directed to not only parenteral but also cosmetic compositions, (see page 27, claims 1, 3-4). Accordingly, using ethanol to form an aqueous dispersion is conventional and dependent on the utility of the formulation (see page 13, 19-23).

Consequently, even though Yiv fails to use ethanol in his composition it would have been obvious to one of ordinary skill in the art at the time of invention to add ethanol into Yiv's carrier system as suggested by Yiv itself and as taught by '192,

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because the ordinary skill in the art would have had a reasonable expectation of success to enhance the delivery of Yiv's active agent to specific tissues, such as dermal tissue, when adding adequate amount of ethanol to Yiv's carrier system, because as taught by '192 use of ethanol improves topical application of the nanodispersion shown by Yiv.

Response to Arguments

Applicant's arguments with filed on December 20, 2002 have been fully considered but are not persuasive. Applicant argues that ethanol used in '192 is an optional excipient, not an essential component. Further, Applicant argues that '192 uses sphingolipids which are not used in the instant claims. Applicant also appears to be arguing that unlike instant claims Yiv teaches injectable drugs wherein propylene glycol is an essential component. Finally, Applicant alleges non-analogous art because Yiv teaches injectable drugs and Weder's compositions are directed to cosmetic formulations.

In response, Examiner first argues that both cited references are directed to microemulsions and nanodispersions which are universally employed in both cosmetic and pharmaceutical art as a suitable delivery system for lipophilic agents. These compositions are essentially used as delivery systems in both cosmetic, parenteral or even oral formulations. In fact, '192 patent sets forth that nanodispersions having such characteristics are used in both cosmetic and parenteral (injectable) formulations, therefore, with respect to their utility, there is extensive overlap in the art of cosmetic and pharmaceutical delivery systems.

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Further, one of ordinary skill in the art would view Yiv and '192's teachings' to be analogous as they solve the same problem in the art, namely facilitating effective delivery of lipophilic agents. In fact, the scope of pending claims are not limited to specific cosmetic or injectable formulations, rather both. Therefore, such arguments are not commensurate with the scope of the pending claims.

Second, Examiner points out that Yiv is used as the primary reference in the rejection under question. Yiv does not use sphingolipids in his compositions. Therefore, the use of sphingolipids in '192 is not relevant, because '192 is merely used to show conventional use of ethanol in nanodispersion delivery systems. Moreover, Yiv specifically teaches the use of lower alcohols such as ethanol in his composition (col 7, lines 10-14) regardless of its essentiality. Therefore, absence of showing unexpected results the ordinary artisan would have had a reasonable expectation of success to use ethanol when suitable. This modification of Yiv's compositions would have been well within the ordinary skill of the artisan, specially since the teachings of '192 provides reasonable expectation of success for the ordinary artisan when ethanol is used as the solvent.

Next, Applicant asserts that propylene glycol of Yiv is an essential component. In response, Examiner states again that the instant claims do not exclude such feature. Specifically, claims 28 and 29, consist essentially of the components (a), (b), (c), and (d). Component (c) is a lipophilic component "**comprising**" a natural or synthetic or partially synthetic triglyceride, and a lipophilic agent. Nowhere is the use of PEG is

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excluded in the pending claims as it can exist in component (c) to facilitate stability.

Therefore, Applicant's arguments are not commensurate with the scope of the claims.

Furthermore, the declaration filed on under Rule 132, Paper No. 29, by Andreas Supersaxo, does not establish unexpected results in compare to formulations with PEG. First, only the species compared in examples 2A and 2B shows relative consistency in homogeneity. The comparative examples 1A and 1B have a standard deviation of about 50%, therefore, no unexpected results can be extrapolated from such results. Further, not enough species are compared to establish an unexpected trend. Finally, assuming *arguendo* that the results submitted establishes homogeneity, it is not clear how such characteristic renders the pending claims patentable over the prior art. The instant claims are not directed to a final homogenous nanodispersion, rather a homogenous mixture obtained in step (α). Further, Yiv teaches filtering his formulation through a 0.22 micron filter, therefore, his final formulations must possess homogeneity at least to the extent that no particle larger than 0.22 micron exists in his composition.

Finally, Examiner points out that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, dwelling on the shortcomings of the cited references does not remedy the obviousness of the pending claims as a whole. The teachings of cited references must be viewed in their entirety. Examiner points out that all elements of the claims are taught in the cited references, accordingly, the rejection is proper because their combined teachings meets all the

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limitations of the instant claims. Applicant has failed to draw a clear line between the compositions of prior art and those instantly claimed. Therefore, the rejection is maintained.

Conclusion

No claims are allowed.

This is a continued examination of applicant's earlier Application No. 09/306,006. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

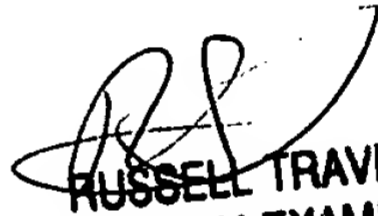
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 703-306-5400. The examiner can normally be reached on 8:30 am - 6:00 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 703-308-1877. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.

SS
April 19, 2003


RUSSELL TRAVERS
PRIMARY EXAMINER
GROUP 1200